IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Bateman *et al.*	Conf. No.:	3842
Serial No.:	10/699,035	Examiner:	Haddad, M.M.
Filed:	October 31, 2003	Group Art Unit:	1644
For:	A MOLECULAR MARKER		

PRE-APPEAL REQUEST FOR REVIEW

April 23, 2007

Mailstop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The following Pre-Appeal Brief Request for Review ("Request") is being filed in accordance with the provisions set forth in the Official Gazette Notice of July 12, 2005 ("OG Notice"). Pursuant to the OG Notice, this Request is being filed concurrently with a Notice of Appeal. This Request is accompanied by a petition for a one (1)-month extension of time and the requisite fee under 37 C.F.R. § 1.17(a)(1). With the extension, this Request is due April 23, 2007 (April 21, 2007 falling on a Saturday).

The Applicants respectfully request reconsideration of the Application in light of the remarks set forth below.

REMARKS

Applicants contend that the rejection of claims 4-5, 12 and 43-44 contain clear legal and/or factual deficiencies, as described below. In a final Office Action, dated December 21, 2006, claims 4-5, 12 and 43-44 were rejected under 35 U.S.C. § 112, first paragraph, as (1) allegedly not supported by either a specific and/or substantial asserted utility or a well-established utility, such that one skilled in the art would not know how to make and use the claimed invention, and (2) failing to meet the written description requirement. The Advisory Action, mailed April 2, 2007, maintained the rejections, but, for purposes of appeal, entered the claim amendments. Applicants request a finding that these rejections are improper and allowance of these claims.

The Office Action contends that the specification does not provide guidance as to how the skilled artisan would measure WARP for extracellular matrix (ECM) integrity. The Office Action further contends that, among other things, the specification does not provide sufficient guidance as to the nature of the changes made to a reference WARP sequence for the skilled artisan to make and use such "derivative" and "homolog." In Applicants' response to the final Office Action, Applicants amended claim 4 to delete the phrase "or a derivative or homolog thereof which in situ forms part of the extracellular matrix (ECM) in an animal."

With respect to the contention of the Office Action that the claims lack a specific and substantial utility, Applicants note: the claims do not recite the use of a polypeptide of the invention as a marker for ECM integrity. Thus, a showing of the correlation of WARP with ECM integrity is not necessary. Nonetheless, the polypeptide of the instant invention has a substantial and specific utility as a histological marker. Such utility is disclosed throughout the specification, for example, in paragraph [0002] of patent publication No. US2004-0214349 ("the '349 publication"), "the present invention provides a molecular marker of cartilage integrity. The *identification of the molecular marker in circulatory or tissue fluid is indicative of disrepair of the extracellular matrix* and in particular cartilage such as caused or facilitated by trauma or a degenerative disease or other condition, for example, arthritis or autoimmunity, specifically, a histological marker for cartilage" (emphasis added).

Paragraph [0007] of the '349 publication discloses that "both WARP and WARP represent molecular markers of ECM and in particular cartilage integrity. The presence or absence of WARP or altered levels of WARP relative to normal controls is proposed to be indicative of disease conditions such as arthritis or cartilage disease." The specification further discloses that a loss of ECM integrity can be detected "by screening body fluid from the animal for the presence of a WARP fragment thereof wherein the presence of the WARP or fragment is indicative of a loss of ECM integrity. See also paragraph [0022] of the '349 publication ("the identification of WARP permits the detection of mutations in WARP such as those involved in disease conditions such as cartilage disease or arthritis or in a propensity for the development of disease conditions. WARP expression may also be a sensitive indicator of cartilage cell differentiation and is proposed to be useful in monitoring repair, regeneration or other disease processes in a subject. Furthermore, WARP may be used to condition or stabilize stem cells in order to facilitate imprinting of stem cells for tissue replacement therapy.").

Applicants submit that detecting WARP in circulating or tissue fluid is a clear indication of disrepair of the ECM. Moreover, the specification discloses how to detect WARP expression, for instance by Western blot and Northern blot. See, for example, Figure 3, Examples 4 and 12, and paragraphs [0149], [0150] of the '349 publication, as discussed in Applicants' response filed March 21, 2007, pages 5-6.

Further, as discussed in the March 21, 2007 response, page 6, Figure 5 and Example 6 shows that WARP is expressed in newborn mouse cartilage. "[T]he results clearly show that WARP is also found in the cartilage matrix in vivo, and the necessity for extraction with a chaotrophic agent suggests that it may be a strongly interacting matrix component." Paragraph [0154]. Given the need for a chaotropic agent to extract WARP from cartilage matrix further support Applicants position that, detecting WARP in a circulatory or tissue fluid is indicative of matrix disrepair.

Thus, Applicants submit that the specification provides support for the utility of WARP for identifying these cells using the WARP polypeptide of the instant invention. Moreover, based on the expression profile of WARP, Applicants respectfully submit that any number of specific and substantial utilities for WARP as described in the specification stem

directly from its chondrocyte cell and cartilage tissue-specific expression profile. Applicants respectfully submit that the claimed invention is supported by at least a specific and substantial asserted utility such that one ordinarily skilled in the art would appreciate the diagnostic utilities of the WARP polypeptides and know how to use the claimed invention. Accordingly, Applicants respectfully request that the Examiner withdraw the rejections of claims 4-5, 12 and 43-44 under 35 U.S.C. § 112, first paragraph.

Applicants further submit that the claims meet the written description requirement. The Office Action contends that there is no described or art-recognized correlation or relationship between the structure of the invention, the Willebrand domain of the WARP and its function in the ECM. Thus, the Office Action contends, that one of skill in the art would not envisage, based on the disclosure, the claimed genus or derivative, homolog, 95% or 99% similarity to SEQ ID NO:5, which retain the features essential to the present invention.

Applicants have amended claims 4 and 43 in the March 21, 2007 response, to delete, without prejudice, the recitation of the phrase "or a derivative or homolog thereof which *in situ* forms part of the extracellular matrix (ECM) in an animal." As amended, Applicants submit that the rejection of the terms "derivative" or "homolog" is moot.

With respect to the claimed features of "95% homology" and "99% homology," Applicants respectfully submit that the specification provides ample support for the terms. The specification in paragraph [0051] defines "homolog" as including "an analogous polypeptide having at least about 65% similar amino acid sequence from another animal species or from a different locus within the same species." Further, as disclosed in paragraph [0144] of the specification, "[t]he human homolog of WARP was identified by searching the genome data with the mouse WARP protein sequence. A match with a predicted protein sequence (hypothetical protein FLJ22215) with very high homology to the mouse WARP was found. ... These sequences are clearly homologs of each other because they share 79% amino acid identity (see FIG. 1C). In addition, if conserved changes are considered in the analysis, they share 95% identity."

Applicant further submits that the Office Action is incorrect in that an insufficient number of species are disclosed. Applicants disclose a human and a mouse WARP protein. Areas of sequence identity and similarity are shown in Figure 1C. Given that Applicants provide written description for "homolog" and a mouse and a human WARP sequence that are 79% identical, or 95% identical of conserved amino acids are considered, Applicants respectfully submit that the presently amended claims satisfy the written description requirement. Accordingly, Applicant respectfully requests that the Examiner withdraw the rejections of claims 4-5, 12 and 43-44 under 35 U.S.C. § 112, first paragraph.

Conclusion

As the rejection of claims 4, 5, 12 and 43-44 contains clear factual and/or legal deficiencies, Applicants respectfully request a finding of allowance of claims 4, 5, 12 and 43-44. If the United States Patent and Trademark Office deems that an interview is appropriate, Applicants would appreciate the opportunity for such an interview. To the extent not already provided, the Director is hereby authorized to charge any required fees or credit any overpayments to Deposit Account 02-4377 of Baker Botts, LLP.

Respectfully submitted,

By: _____

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